

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
(DOCKET NO. API-02-13-US)**

In the application of:	)	
	)	Examiner: Wu Cheng Winston Shen
Astsaturov, et al.	)	
	)	Art Unit: 1632
Application No.: 10/690,199	)	
	)	
Filed: 10/21/2003	)	
	)	
Title: VACCINES USING HIGH-DOSE	)	
CYTOKINES	)	

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450  
*Submitted via EFS-Web*

**INFORMATION DISCLOSURE STATEMENT**

Applicants respectfully submit this Information Disclosure Statement, PTO-1449 and copies of the reference cited therein. The undersigned hereby authorizes the Commissioner to deduct the required \$180.00 fee (37 CFR 1.17(p)) and any other required fees from Deposit Account No. 50-0244.

This Information Disclosure Statement is in compliance with the duty of candor as set forth in 37 C.F.R. § 1.56. It is requested that the documents be given careful consideration and that they be cited of record in the prosecution history of the present application so that they will appear on the face of the patent issuing of the present application. In the judgment of the undersigned, portions of the references may be material to the examination of the pending claims. However, the references have not been reviewed in sufficient detail to make any other representation and, in particular, no representation is intended as to the relative importance of any portion of the references. This Statement is not a representation that the cited references have effective dates early enough to be "prior art" within the meaning of 35 U.S.C. §102 or §103.

## U.S. Patents

4,923,808  
5,093,258  
5,141,742  
5,342,774  
5,405,940  
5,462,871  
5,505,941  
5,554,724  
5,585,461  
5,591,430  
5,679,647  
5,686,068  
5,695,994  
5,698,530  
5,804,566  
5,830,877  
5,831,016  
5,840,839  
5,844,075  
5,851,523  
5,871,727  
5,874,560  
5,942,235  
5,965,535  
5,972,597  
5,985,847  
6,001,349  
6,025,474  
6,037,135  
6,045,802  
6,083,703  
6,087,110  
6,127,116  
6,132,980  
6,228,621  
6,245,333  
6,319,496  
6,340,462  
6,407,063  
6,511,800  
6,531,451  
6,548,068  
6,558,671  
6,537,560

6,599,699  
6,656,734B1  
6,693,086  
6,699,475  
6,756,038  
6,780,407  
6,710,172  
6,805,869  
6,893,869  
6,951,917  
6,969,609  
7,211,432  
7,255,862  
7,232,887  
7,364,729  
2001/0007659A1  
2002/0123471A1  
2003/0022854A1  
2003/0082150A1  
2003/0113919A1  
2004/003323A1  
2004/0091995A1  
2004/0146485A1  
2004/0156861A1  
2005/0136066A1  
09/693,755

**Non-U.S. Patent Documents**

EP 1074267A1  
WO 87/04076A  
WO 91/11194A1  
WO 92/01796  
WO 92/21376A1  
WO 96/11279  
WO 97/15597A1  
WO 98/15636  
WO 98/04728A1  
WO 98/29556A1  
WO 99/18992A1  
WO 99/19501  
WO 99/18992A  
WO 99/30742A1  
WO 99/40188A2  
WO 99/43839A1  
WO 99/46992A1

WO 99/46988  
WO 01/75117A2  
WO 01/75016A2  
WO 01/30382A1  
WO 01/30847A1  
WO 03/080800A2

### **Non-Patent Documents**

AARTS, et al. Vector-based Vaccine/Cytokine Combination Therapy to Enhance Induction of Immune Responses to a Self-Antigen and Antitumor Activity. *Cancer Res.* 62: 5770-5777 (Oct. 15, 2002)

ABRAMOVICH, et al. Low Dose Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF) and Interleukin-2 (IL-2) Are Well Tolerated Following Autologous Stem Cell Transplant (ASCT) in Patients (pts) with Hematologic-Malignancies. 1999 ASCO Annual Meeting, Abstract 205 (1999)

AHLERS, et al. Mechanisms of Cytokine Synergy Essential for Vaccine Protection Against Viral Challenge. *Int. Immunol.* 13(7): 897-908 (2000)

ANTON, et al. Cytokines and Tumor Vaccination. *Cancer Biotherapeutics and Radiopharmaceuticals.* 11(5): 315-318 (1996)

ARCH, et al. Hypopigmentation associated with an adenovirus-mediated gp100/MART-1 transduced dendritic cell vaccine for metastatic melanoma. *Arch. Dermatol.* 138(6): 799-802 (2002)

ASTSATUROV, et al. Amplification of Virus-Induced Antimelanoma T-Cell Reactivity by High-Dose Interferon-Alpha 2b; Implications for Cancer Vaccines. *Clin. Cancer Res.* 9(12): 4347-4355 (2003)

BAKKER, et al. Analogues of CTL Epitopes with Improved MHC Class-I Binding Capacity Elicit Anti-Melanoma CTL Recognizing the Wild-Type Epitope. *Int. J. Cancer* 70, 302-309 (1997)

BALCH, et al. Final version of the American Joint Committee on Cancer staging system for cutaneous melanoma. *J. Clin. Oncol.* 19: 3635-3648 (2001)

BELARDELLI, et al. The Neglected Role of Type I Interferon in The T-Cell Response: Implications for its Clinical Use. *Immunol. Today,* 17: 369-372 (1996)

BERINSTEIN, et al. Carcinoembryonic Antigen as a Target for Therapeutic Anticancer Vaccines: A Review. *J. Clin. Oncol.* 20(8): 2197-2207 (2002)

BOEL, et al. BAGE: A New Gene Encoding an Antigen Recognized on Human Melanomas by Cytolytic T Lymphocytes. *Immunity,* 2: 167-175 (1995)

BOON, et al. Tumor Antigens Recognized by T Lymphocytes. *Ann. Rev. Immunol.* 12:337-365 (1994)

BOSSIO, et al. Seven Days of Low-Dose Orally Administered Murine Type I Interferon Does Not Cause Priming *In Vivo*. *J. Interferon & Cytokine Res.* 21(7): 463-467 (2001)

BRASSEUR, et al. Human Gene MAGE-1, Which Codes for a Tumor Antigen, is Expressed by Some Breast Tumors. *Int. J. Cancer* 52: 839-841 (1992)

BRASSEUR, et al. Expression of MAGE Genes in Primary and Metastatic Cutaneous Melanoma. *Int. J. Cancer* 63: 375-380 (1995)

BUELER, et al. Induction of Antigen-Specific Tumor Immunity by Genetic and Cellular Vaccines against MAGE: Enhanced Tumor Protection by Coexpression of Granulocyte-Macrophage Colony-Stimulating Factor and B7-1. *Mol. Medicine,* 2(5): 545-555 (1996)

CHAMBERLAIN, et al. Costimulation Enhances the Active Immunotherapy Effect of Anticancer Vaccines. *Cancer Res.* 56: 2832-2836 (1996)

CHAUX, et al. Five MAGE-A1 Epitopes Recognized by Cytolytic T Lymphocytes Obtained by In Vitro Stimulation with Dendritic Cells Transduced with MAGE-A1. *J. Immunol.* 163: 2928-2936 (1999)

CHEN, et al. Recombinant interferon alpha can induce rearrangement of T-cell antigen receptor alpha-chain genes and maturation to cytotoxicity in T-lymphocyte clones in vitro. *PNAS U.S.A.* 83: 4887-4889 (1986)

CHO, et al. IFN- $\alpha\beta$  Promote Priming of Antigen-Specific CD8+ and CD4+ T Lymphocytes by Immunostimulatory DNA-Based Vaccines. *J. Immunol.* 168: 4907-4913 (2002)

CHOMEZ, et al. The SMAGE Gene Family is Expressed in Post-Meiotic Spermatids During Mouse Germ Cell Differentiation. *Immunogenetics* 43: 97-100 (1996)

COX, et al. Identification of a Peptide Recognized by Five Melanoma-Specific Human Cytotoxic T Cell Lines. *Science*, vol. 264: 716-719 (1994)

COULIE, et al. A Mutated Intron Sequence Codes for an Antigenic Peptide Recognized by Cytotoxic T Lymphocytes on a Human Melanoma. *PNAS USA*, 92: 7976-7980 (1995)

DE PLAEN, et al. Structure, Chromosomal Localization, and Expression of 12 Genes of the MAGE Family. *Immunogenetics* 40: 360-369 (1994)

DE SMET, et al. Sequence and Expression Pattern of the Human MAGE2 Gene. *Immunogenetics* 39:121-129 (1994)

DISIS, et al. Granulocyte-Macrophage Colony-Stimulating Factor: An Effective Adjuvant for Protein and Peptide-Based Vaccines. *Blood*, 88(1): 202-210 (1996)

DUBENSKY, et al. Delivery Systems for Gene-Based Vaccines. *Mol. Med.* 6(9): 723-732 (2000)

ELLEM, et al. The labyrinthine ways of cancer immunotherapy--T cell, tumor cell encounter: "how do I lose thee? Let me count the ways". *Adv. Cancer Res.* 75:203-49: 203-249 (1998)

EURA, et al. Expression of the MAGE Gene Family in Human Squamous Cell Carcinomas. *Int. J. Cancer* 64: 304-308 (1995)

FUJIE, et al. A MAGE-1-Encoded HLA-A24-Binding Synthetic Peptide Induces Specific Anti-Tumor Cytotoxic T Lymphocytes. *Int. J. Cancer* 80: 169-172 (1999)

GAUGLER, et al. Human gene MAGE-3 codes for an antigen recognized on a melanoma by autologous cytolytic T lymphocytes. *J. Exp. Med.* 179: 921-930 (1994)

GRAMAGLIA, et al. Ox-40 Ligand: A Potent Costimulatory Molecule for Sustaining Primary CD4 T Cell Responses. *J. Immunol.* 161: 6510-6517 (1998)

GROB, et al. Interferon as an adjuvant for Hepatitis B Vaccination in Non- and Low-Responder Populations. *Eur. J. Clin. Microb.* 3(3): 195-198 (1984)

GURUNATHAN, et al. CD40 Ligand/Trimer DNA Enhances Both Humoral and Cellular Immune Responses and Induces Protective Immunity to Infectious and Tumor Immunity. *J. Immunol.* 161: 4563-4571 (1998)

HALUSKA, et al. Immunologic Gene Therapy: A Phase I/II Trial Utilizing Autologous Dendritic Cells Transduced with gp100 and Melan A/MART-1-Encoding Adenoviruses in Advanced Melanoma. *Blood*, 98(1): 694a-695a, Abstract 2903 (Nov. 16, 2001)

HEINTEGES, et al. Combination Therapy of Active HBSAG Vaccination and Interferon-Alpha in Interferon-Alpha Nonresponders with Chronic Hepatitis B. *Digestive Diseases and Sciences*, 4(46): 901-906 (2001)

HERMAN, et al. A Peptide Encoded by the Human MAGE3 Gene and Presented by LA-B44 Induces Cytolytic T Lymphocytes That Recognize MAGE3. *Immunogenetics* 43: 377-383 (1996)

HERMONAT, et al. Use of Adeno-Associated Virus as a Mammalian DNA Cloning Vector: Transduction of Neomycin Resistance Into Mammalian Tissue Culture Cells. *PSNA USA*, 81: 6466-6470 (1984)

HERZ, et al. Adenovirus-Mediated Transfer of Low Density Lipoprotein Receptor Gene Acutely Accelerates Cholesterol Clearance in Normal Mice. *PNAS USA*, 90: 2812-2816 (1993)

HODGE, et al. Admixture of Recombinant Vaccinia Virus Containing the Gene for the Costimulatory Molecule B7 and a Recombinant Vaccinia Virus Containing a Tumor-associated Antigen Gene Results in Enhanced Specific T-Cell Responses and Antitumor Immunity. *Cancer Res.* 55: 3598-3603 (1995)

HODGE, et al. Diversified Prime and Boost Protocols Using Recombinant Vaccine Virus and Recombinant Non-Replicating Avian Pox Virus to Enhance T-Cell Immunity and Antitumor Responses. *Vaccine*, vol. 15, issue 6/7, pp. 759-768 (1997)

HODGE, et al. A Triad of Costimulatory Molecules Synergize to Amplify T-Cell Activation. *Cancer Res.* 59: 5800-5807 (1999)

HORIG, et al. Phase I Clinical Trial of Recombinant Canarypox (ALVAC) Vaccine Expressing Human Carcinoembryonic Antigen and B7.1 Costimulatory Molecule. *Cancer Immunol. Immunother.* 49: 504-514 (2000)

HU, et al. Enhancement of T Lymphocyte Precursor Frequency in Melanoma Patients Following Immunization with the MAGE-1 Peptide Loaded Antigen Presenting Cell-Based Vaccine. *Cancer Res.* 56: 2479-2483 (1996)

HURPIN, et al. The Mode of Presentation and Route of Administration Are Critical for the Induction of Immune Responses to p53 and Antitumor Immunity. *Vaccine*, vol. 16, no. 2/3, pp. 208-215 (1998)

IL2 Therapy : Low Dose Daily vs. High Dose Intermittent Regimens. Author Unknown. (2001)

INOUE, et al. Human Esophageal Carcinomas Frequently Express the Tumor-Rejection Antigens of MAGE Genes. *Int. J. Cancer* 63: 523-526 (1995)

IRVINE, et al. Recombinant Virus Vaccination Against "Self" Antigens Using Anchor-Fixed Immunogens. *Cancer Res.*, vol. 59: 2536-2540 (1999)

KARAKINAS, et al. Monoclonal Anti-MAGE-3 CTL Responses in Melanoma Patients Displaying Tumor Regression after Vaccination with a Recombinant Canarypox Virus. *J. Immunol.* 171: 4989-4904 (2003)

KAWAKAMI, et al. Identification of a Human Melanoma Antigen Recognized by Tumor-Infiltrating Lymphocytes Associated with in vivo Tumor Rejection. *Proc. Natl. Acad. Sci. USA*, vol. 91, pp. 6458-6462 (1994)

KAWAKAMI, et al. Identification of the Immunodominant Peptides of the MART-1 Human Melanoma Antigen Recognized by the Majority of HLA-A2-restricted Tumor Infiltrating Lymphocytes. *J. Exp. Med.* 180: 347-352 (1994)

KAWASHIMA, et al. The Multi-epitope Approach for Immunotherapy for Cancer: Identification of Several CTL Epitopes from Various Tumor-Associated Antigens Expressed on Solid Epithelial Tumors. *Human Immunol.* 59: 1-14 (1998)

KIRKWOOD, et al. Interferon Alfa-2b Adjuvant Therapy of High-Risk Resected Cutaneous Melanoma : The Eastern Cooperative Oncology Group Trial EST 1684. *J. Clin. Oncol.* 14(1): 7-17 (1996)

KIRKWOOD, et al. Systemic Adjuvant Treatment of High-Risk Melanoma: the Role of Interferon Alfa-2b and Other Immunotherapies. *Eur. J. Cancer*, 34: 12-17 (1998)

KIRKWOOD, et al. High- and Low-Dose Interferon Alfa-2b in High-Risk Melanoma: First Analysis of Intergroup Trial E1690/S9111/C9190. *J. Clin. Oncol.* 18(12): 2444-2458 (2000)

KIRKWOOD, et al. High-Dose Interferon Alfa-2b Does Not Diminish Antibody Response to GM2 Vaccination in Patients With Resected Melanoma: Results of the Multicenter Eastern Cooperative Oncology Group Phase II Trial E2696. *J. Clin. Oncol.* 19: 1430-1436 (2001)

KIRKWOOD, et al. High-Dose Interferon Alfa-2b Significantly Prolongs Relapse-Free and Overall Survival Compared With the GM2-KLH/QS-21 Vaccine in Patients With Resected Stage IIB-III Melanoma: Results of Intergroup Trial E1694/S9512/C509801. *J. Clin. Oncol.* 19: 2370-2380 (2001)

KOCHER, et al. Identification and Intracellular Location of MAGE-3 Gene Product. *Cancer Res.* 55: 2236-2239 (1995)

KUNDIG, et al. Fibroblasts as Efficient Antigen-Presenting Cells in Lymphoid Organs. *Science*, 268: 1343-1347 (1995)

KURZROCK, et al. Pilot Study of Low-Dose Interleukin-11 in Patients With Bone Marrow Failure. *19(21): 4165-4172 (2001)*

LE BON, et al. Type I Interferons Potently Enhance Humoral Immunity and Can Promote Isotype Switching by Stimulating Dendritic Cells In Vivo. *Immunity*, 14: 461-470 (2001)

LEITNER, et al. Enhancement of Tumor-Specific Immune Response with Plasmid DNA Replicon Vectors. *Cancer Res.* 60: 51-55 (2000)

LINDSEY, et al. Impact of the Number of Treatment Courses on the Clinical Response of Patients Who Receive High-Dose Bolus Interleukin-2. *J. Clin. Oncol.* 18(9): 1954-1959 (2000)

LIU, et al. Gene-Based Vaccines. *Mol. Ther.* 1(6): 497-500 (2000)

LUDWIG, et al. Should Alpha-Interferon be Included as Standard Treatment in Multiple Melanoma? *Eur. J. Cancer*, 34: 12-24 (1998)

MAEURER, et al. New Treatment Options for Patients with Melanoma: Review of Melanoma-Derived T-Cell Epitope-Based Peptide Vaccines. *Melanoma Res.* 6: 11-24 (1996)

MARRACK, et al. Type I Interferons Keep Activated T cells Alive. *J. Exp. Med.* 189: 521-530 (1999)

MARCHAND, et al. Tumor Regressions Observed in Patients with Metastatic Melanoma Treated with an Antigenic Peptide Encoded by Gene MAGE-3 and Presented by HLA-A1. *Int. J. Cancer.* 80: 219-230 (1999)

MARSHALL, et al. Phase I Study in Advanced Cancer Patients of a Diversified Prime-and-Boost Vaccination Protocol Using Recombinant Vaccinia Virus and Recombinant Nonreplicating Avipox Virus to Elicit Anti-Carcinoembryonic Antigen Immune Responses. *J. Clin. Oncol.* 18, 3964-3973 (2000)

MARSHALL, J. Carcinoembryonic Antigen-Based Vaccines. *Semin. Oncol. (suppl. 8): 30-36 (2003)*

MATEO, et al. An HLA-A2 Polypeptide Vaccine for Melanoma Immunotherapy. *J. Immunol.* 163(7): 4058-4063 (1999)

MILLER, et al. Targeted Vectors for Gene Therapy. *FASEB J.* 9: 190-199 (1995)

MOINGEON, et al. Cancer Vaccines. 19: 1305-1326 (2001)

NAGAO, et al. Oral-Mucosal Administration of Interferon-Alpha Potentiates Immune Response in Mice. *J. Int. Cyt. Res.* 18(9): 661-666 (1998)

NESTLE, et al. Vaccination of Melanoma Patients with Peptide- or Tumor Lysate-Pulsed Dendritic Cells. *Nature Med.* Vol. 4, No. 3, pp. 328-332 (1998)

OERTLI, et al. Rapid Induction of Specific Cytotoxic T Lymphocytes Against Melanoma-Associated Antigens by a Recombinant Vaccinia Virus Vector Expressing Multiple Immunodominant Epitopes and Costimulatory Molecules *In Vivo*. *Human Gene Therapy*, 13(4): 569-575 (March 2002)

PARDOLL, D.M. Cancer Vaccines. *Nat.Med.* 4: 525-531 (1998)

PARKHURST, et al. Improved Induction of Melanoma-Reactive CTL with Peptides from Melanoma Antigen gp100 Modified at HLA-A0201-Binding Residues. *J. Immunol.* Vol. 157, no. 6, pp. 2539-48 (1996)

PARMIANI, et al. Cancer Immunotherapy with Peptide-Based Vaccines: What Have We Achieved? Where Are We Going? *J. Natl. Cancer Inst.* 94: 805-818 (2002)

PATARD, et al. Expression of MAGE Genes in Transitional Cell Carcinomas of the Urinary Bladder. *Int. J. Cancer* 64: 60-64 (1995)

PHAN, et al. Factors Associated with Response to High-Dose Interleukin-2 in Patients with Metastatic Melanoma. *J. Clin. Oncol.* 19(15): 3477-3482 (2001)

PHAN, et al. Cancer Regression and Autoimmunity Induced by Cytotoxic T Lymphocyte-Associated Antigen 4 Blockade in Patients with Metastatic Melanoma. *PNAS USA*, 100(14): 8372-8377 (2003)

QUENTIN, et al. Adenovirus as an Expression Vector in Muscle Cells *in vivo*. *PNAS USA*, 89: 2581-2584 (1992)

RAO, et al. Partial Characterization of Two Subpopulations of T4 Cells Induced by Active Specific Intralymphatic Immunotherapy (ASILI) in Melanoma Patients. Vol. 27, abstract 1290, p. 325 (1986)

RESTIFO, et al. Antigen Processing *In Vivo* and the Elicitation of Primary CTL Responses. *J. Immunol.* 154: 4414-4422 (1995)

ROSENBERG, et al. Immunologic and Therapeutic Evaluation of a Synthetic Peptide Vaccine for the Treatment of Patients with Metastatic Melanoma. *Nature Med.* 4: 321-327 (1998)

ROSENBERG, S.A. Progress in Human Tumour Immunology and Immunotherapy. *Nature* 411, 380-384 (2001)

ROSSI, et al. Hyperthermic Isolated Limb Perfusion with Low-Dose Tumor Necrosis Factor- $\alpha$  and Melphalan for Bulky In-Transit Melanoma Metastases. *Ann. Surg. Oncol.* 11(2): 173-177 (2004)

SALGALLER, et al. Immunization Against Epitopes in the Human Melanoma Antigen gp100 Following Patient Immunization with Synthetic Peptides. *Cancer Res.* Vol. 56, pp. 4749-4757 (1996)

SANTINI, et al. Type I Interferon as a Powerful Adjuvant for Monocyte-Derived Dendritic Cell Development and Activity *In vitro* and in Hu-PBL-SCID Mice. *J. Exp. Med.* 191(10): 1777-1788 (2000)

SCHULTZ, et al. A MAGE-3 Peptide Recognized on HLA-B35 and HLA-A1 by Cytolytic T Lymphocytes. *Tissue Antigens.* 57: 103-109 (2001)

SPAGNOLI, et al. Cytotoxic T-cell Induction in Metastatic Melanoma Patients Undergoing Recombinant Vaccinia Virus-Based Immuno-Gene Therapy. *Recent Results in Cancer Research*, 160: 195-201 (2002)

TAKAHASHI, et al. Identification of MAGE-1 and MAGE-4 Proteins in Spermatagonia and Primary Spermatocytes of Testis. *Cancer Res.* 55: 3478-3482 (1995)

TANZARELLA, et al. Identification of a Promiscuous T-Cell Epitope Encoded by Multiple Members of the MAGE Family. *Cancer Res.* 59: 2668-2674 (1999)



TARTAGLIA, et al. NYVAC: A Highly Attenuated Strain of Vaccinia Virus. *Virology* 188: 217-232 (1992)

TARTAGLIA, et al. Protection of Cats Against Feline Leukemia Virus by Vaccination with a Canarypox Virus Recombinant, ALVAC-FL. *J. Virol.* 67: 2370-2375 (1993)

TARTAGLIA, et al. Therapeutic Vaccines Against Melanoma and Colorectal Cancer. *Vaccine*, 19(17-19): 2571-2575 (2001)

THOMSON, et al. Minimal Epitopes Expressed in a Recombinant Polyepitope Protein are Processed and Presented To CD8+ Cytotoxic T Cells: Implications for Vaccine Design. *PNAS USA*, 92: 5845-5849 (1995)

THOMSON, et al. Recombinant Polyepitope Vaccines for the Delivery of Multiple CD8 Cytotoxic T Cell Epitopes. *J. Immunol.* 157: 822-826 (1996)

THOMSON, et al. Delivery of Multiple CD8 Cytotoxic T Cell Epitopes by DNA Vaccination. *J. Immunol.* 160: 1717-1723 (1998)

TOES, et al. Protective Anti-Tumor Immunity Induced by Vaccination with Recombinant Adenoviruses Encoding Multiple Tumor-Associated Cytotoxic T Lymphocyte Epitopes in a String-of-Beads Fashion. *PNAS USA* 94: 14660-14665 (1997)

TOSO, et al. MAGE-1-Specific Precursor Cytotoxic T-Lymphocytes Present Among Tumor-Infiltrating Lymphocytes from a Patient with Breast Cancer: Characterization and Antigen-specific Activation. *Cancer Res.* 56: 16-20 (1996)

TOUGH, et al. Induction of Bystander T Cell Proliferation by Viruses and Type I Interferon *in vivo*. *Science*, 272: 1947-1950 (1996)

TRAVERSARI, et al. A Nonapeptide Encoded by Human Gene MAGE-1 is Recognized on HLA-A1 by Cytolytic T Lymphocytes Directed Against Tumor Antigen MZ2-E. *J. Exp. Med.* 176: 1453-1457 (1992)

TSAO, et al. Hypopigmentation Associated with an Adenovirus-Mediated gp100/MART-1-Transduced Dendritic Cell Vaccine for Metastatic Melanoma. *Arch. Dermatol.* 138: 799-802 (2002)

TUTING, et al. Autologous Human Monocyte-Derived Dendritic Cells Genetically Modified to Express Melanoma Antigens Elicit Primary Cytotoxic T Cell Responses *in vitro*: Enhancement by Cotransfection of Genes Encoding the TH1 Biasing Cytokines IL-12 and IFN- $\alpha$ . *J. Immunol.* 160: 1139-1147 (1998)

VAN BAREN, et al. Tumoral and Immunologic Response After Vaccination with an ALVAC Virus Encoding MAGE Antigens Recognized by T Cells. *J. Clin. Oncol.* 23(35): 9008-9021 (2005)

VAN DEN EYNDE, et al. New Tumor Antigens Recognized by T Cells. *Curr. Opin. Immunol.* 7: 674-681 (1995)

VAN DEN EYNDE, et al. A New Family of Genes Coding for an Antigen Recognized by Autologous Cytolytic T Lymphocytes on a Human Melanoma. *J. Exp. Med.* 182: 689-698 (1995)

VAN DEN EYNDE, et al. T cell defined tumor antigens. *Curr. Opin. Immunol.* 9, 684-693 (1997)

VAN DEN EYNDE, et al. Tumor Antigens Recognized by T Lymphocytes. *Int. J. Clin. Lab. Res.* 27: 81-86 (1997)

VAN DER BRUGGEN, et al. A Gene Encoding an Antigen Recognized by Cytolytic T Lymphocytes on a Human Melanoma. *Science*, 254: 1643-1647 (1991)

VAN DER BRUGGEN, et al. Autologous Cytolytic T Lymphocytes Recognize a MAGE-1 Nonapeptide on Melanomas Expressing HLA-Cw\* 1601. *Eur. J. Immunol.* 24: 2134-2140 (1994)

VAN DER BRUGGEN, et al. A Peptide Encoded by Human Gene MAGE-3 and Presented by HLA-A2 Induces Cytolytic T Lymphocytes That Recognize Tumor Cells Expressing MAGE-3. *Eur. J. Immunol.* 24: 3038-3043 (1994)

VAN DER BURG, et al. Induction of p53-Specific Immune Responses in Colorectal Cancer Patients Receiving a Recombinant ALVAC-p53 Candidate Vaccine. *Clin. Cancer Res.* 8: 1019-1027 (2002)

VELDERS, et al. Defined Flanking Spacers and Enhanced Proteolysis is Essential for Eradication of Established Tumors by an Epitope String DNA Vaccine. *J. Immunol.* 166: 5366-5373 (2001)

VON MEHREN, et al. Pilot Study of a Dual Gene Recombinant Avipox Vaccine Containing Both Carcinoembryonic Antigen (CEA) and B7.1 Transgenes in Patients with Recurrent CEA-Expressing Adenocarcinomas. *Clin. Cancer Res.* 6: 2219-2228 (2000)

VON MEHREN, et al. The Influence of Granulocyte Macrophage Colony-Stimulating Factor and Prior Chemotherapy on the Immunological Response to a Vaccine (ALVAC-CEA B7.1) in Patients with Metastatic Melanoma. *Clin. Cancer Res.* 7: 1181-1191 (2001)

WANG, et al. Utilization of an Alternative Open Reading Frame of a Normal Gene in Generating a Novel Human Cancer Antigen. *J. Exp. Med.* 186:1131-1140 (1996)

WEYNANTS, et al. Expression of MAGE Genes by Non-Small-Cell Lung Carcinomas. *Int. J. Cancer* 59:826-829 (1994)

WOLFEL, et al. Two Tyrosine Nonapeptides Recognized on HLA-A2 Melanomas by Autologous Cytolytic T Lymphocytes. *Eur. J. Immunol.* Vol. 24, pp. 759-764 (1994)

XIANG, et al. An Autologous Oral DNA Vaccine Protects Against Murine Melanoma. *Proc. Natl. Acad. Sci. USA*, vol. 97, no. 10, pp. 5492-5497 (2000)

YANG, et al. Randomized Comparison of High-Dose and Low-Dose Intravenous Interleukin-2 for the Therapy of Metastatic Renal Cell Carcinoma: an Interim Report. *J. Clin. Oncol.*, 12: 1572-1576 (1994)

Respectfully Submitted,

Date: March 22, 2010

/Patrick J. Halloran/  
Patrick J. Halloran  
Reg. No. 41,053

Patrick J. Halloran, Ph.D., J.D.  
3141 Muirfield Road  
Center Valley, PA 18034  
Tel: 610-984-4751  
Fax: 484-214-0164  
Email: pat@pathhalloran.com